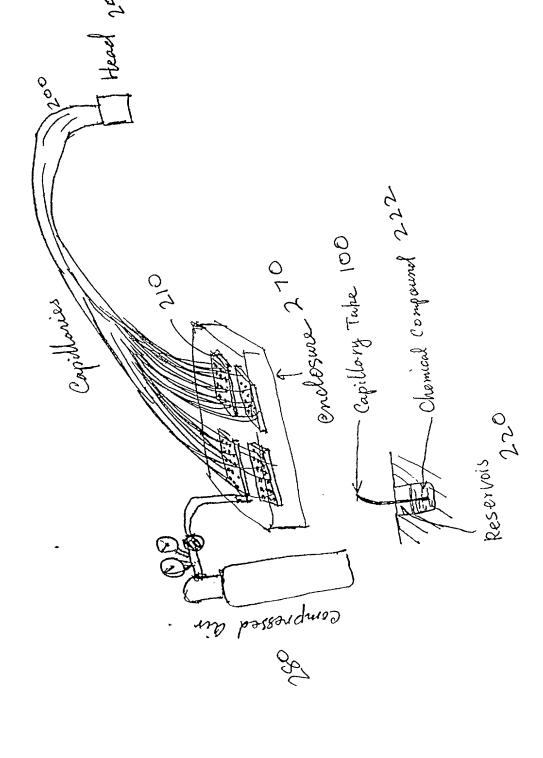


FOR HIGH THROUGHPUT SCREENING
THE: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES

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XHTS

210 097 Imaging Pressure chamber Compound library in microtiter plates 270 -- Microarrays and Fiber Bundles FlG. 2B assay 230 9 200 220 220

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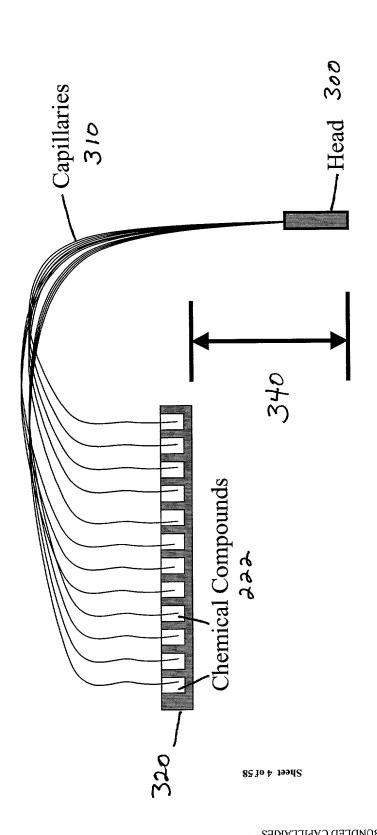


Figure 3

Title: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES POR HIGH THROUGHPUT SCREENING Inventor: Jiannning XIAO et al. Application No.: To Be Assigned Docket No.: 473532000620

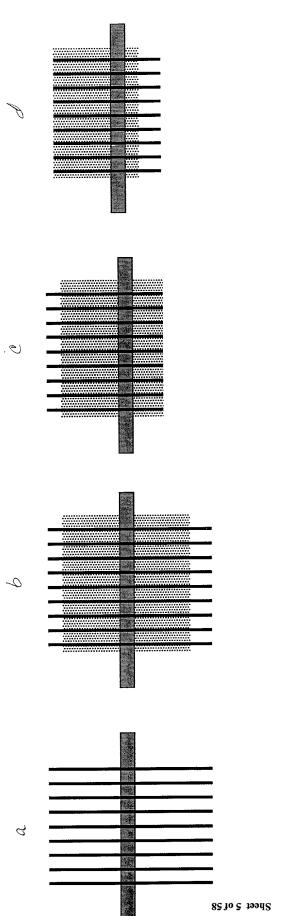


Fig. 4. Fabrication of delivery head using a guide plate

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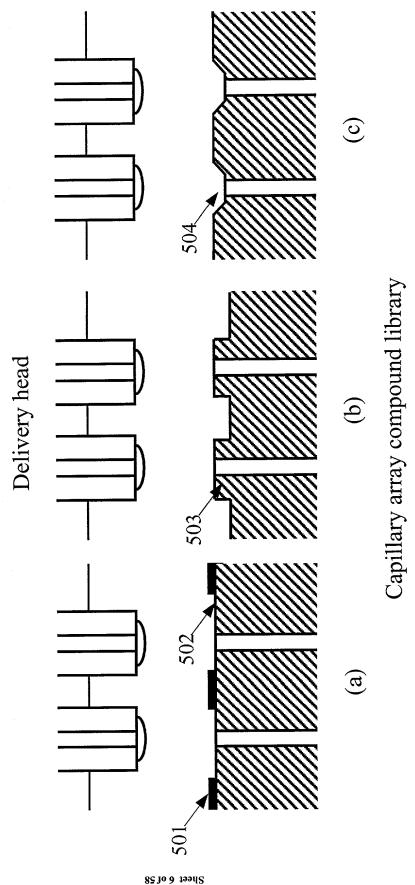


Fig. 5. Surface features on the surface of the capillary array compound library to prevent crosscontamination during compound loading

501 - Hydrophobic coating

502 – Hydrophilic coating

503 - Island

504 - Well

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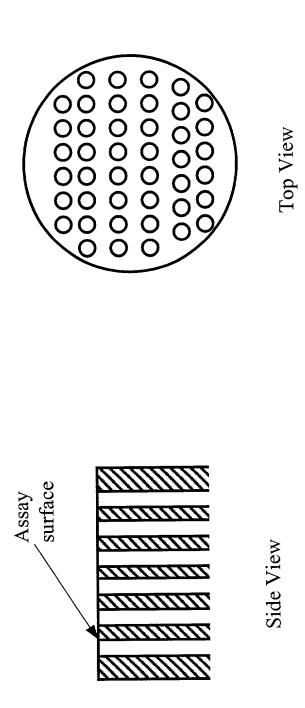


Fig. 6. Basic configuration of capillary array substrate for the portable compound library

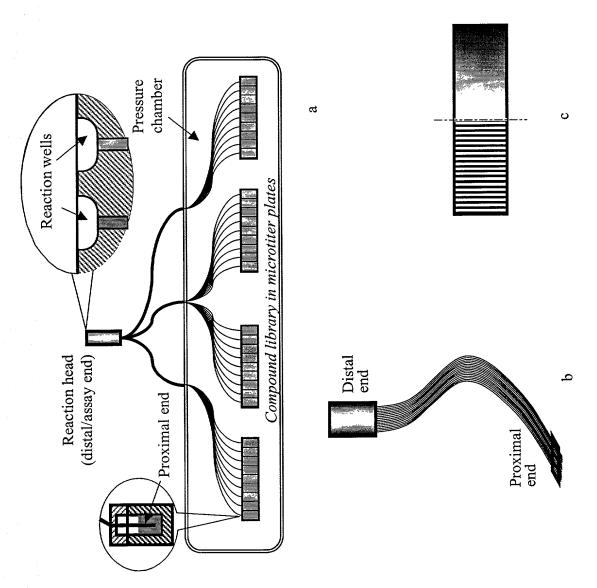
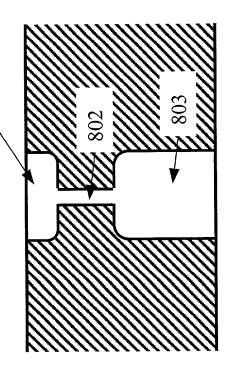


Fig. 7 The capillary array compound library in different formats

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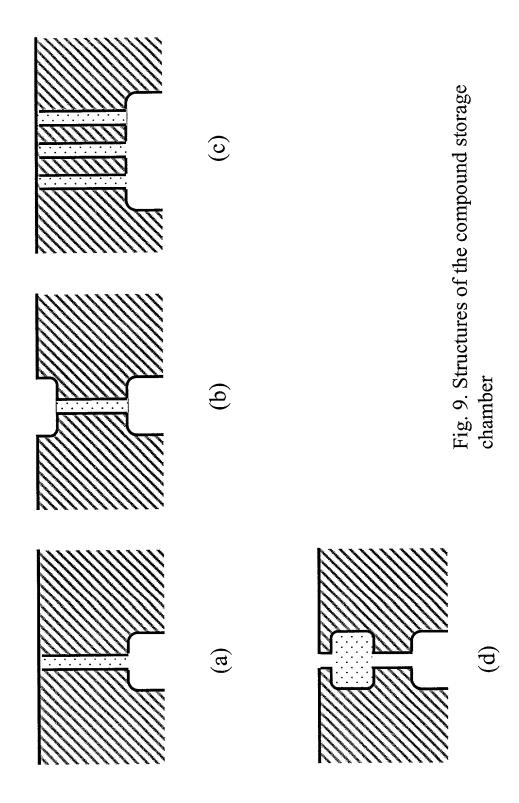
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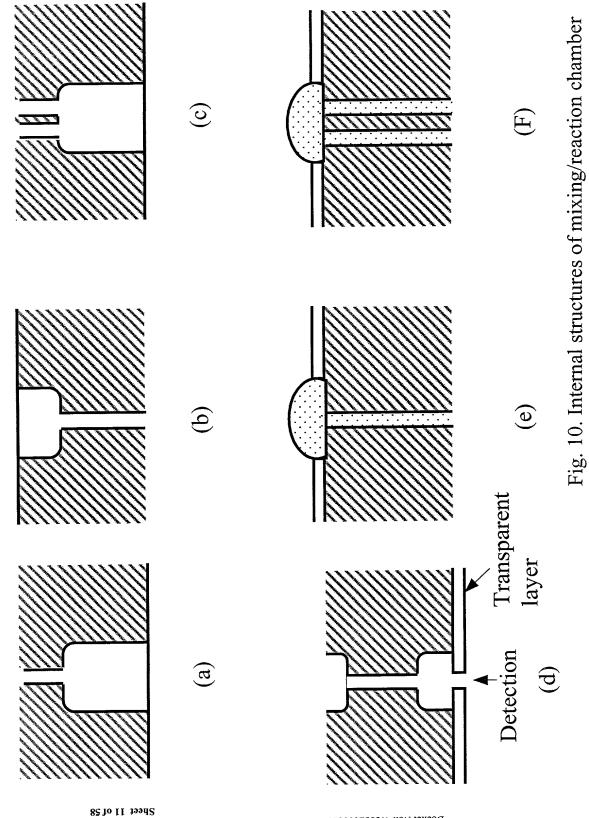


802 - Flow regulator for reagent metering 801 - Mixing/reaction well 803 - Compound reservoir

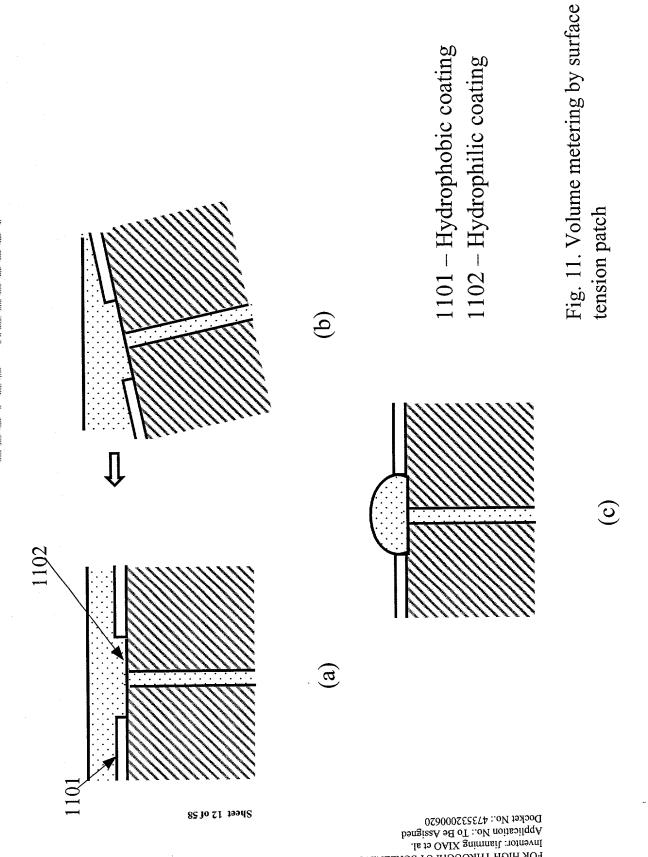
Fig. 8. Internal structure of a through hole in capillary array compound library



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Title: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES

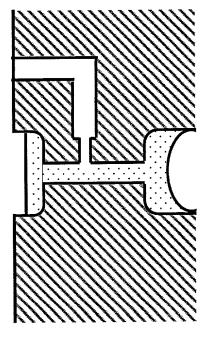
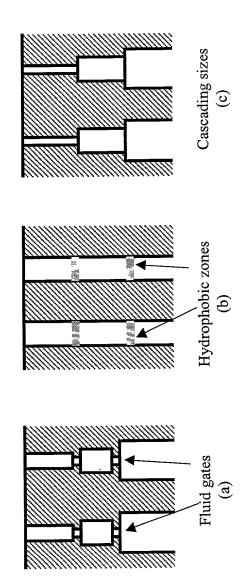


Fig. 12. Fluid regulator with side air tunnel

Fig. 13 Internal through hole structures to facilitate chamber volume metering and mixing



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Fig. 14 Process of metering multiple reagents using interconnected chambers

<u>છ</u> \mathfrak{E} (e) **(P**) 9 (a)

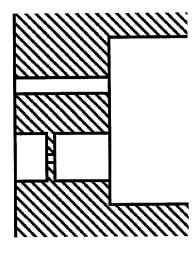
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Fig. 15 Special through hole structure where multiple chambers links to a chamber in parallel



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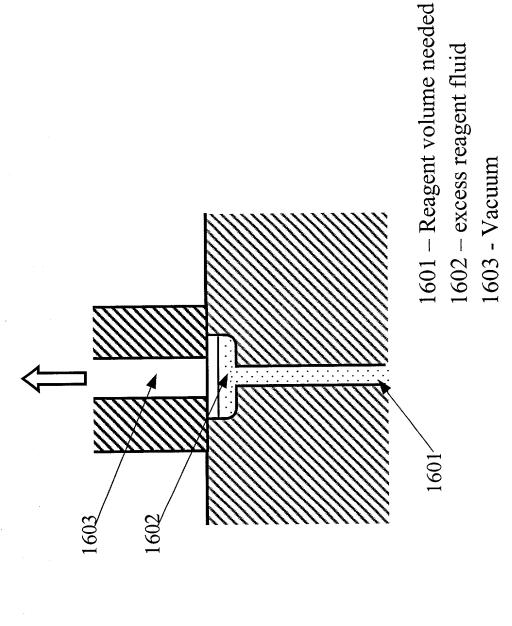


Fig.16. Removal of excess fluid by vacuum

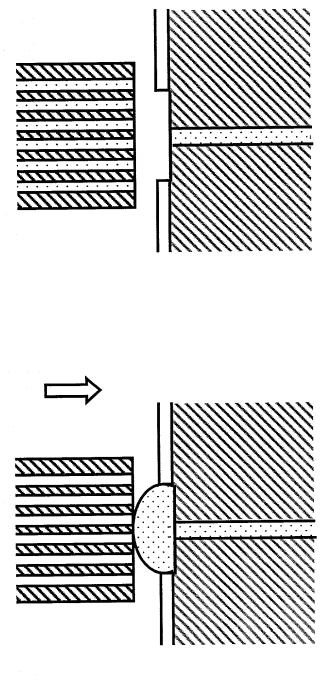
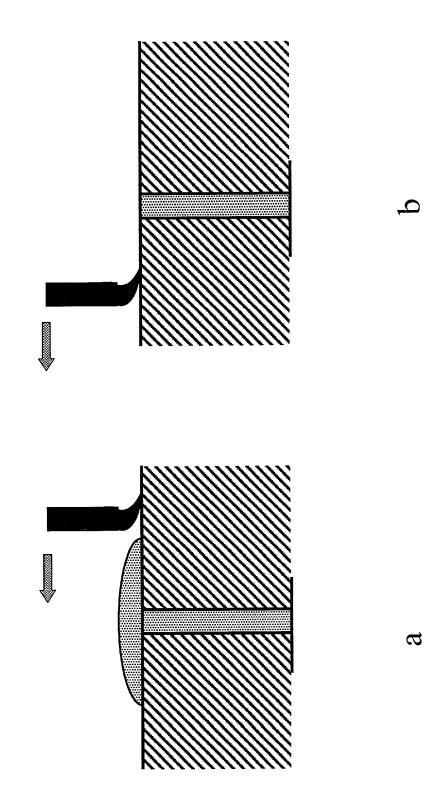


Fig. 17. Excess fluid removal using a second capillary array

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Fig. 18. Excess Fluid Removal by Wiping



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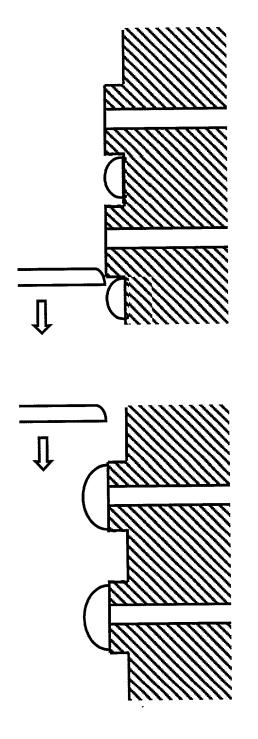
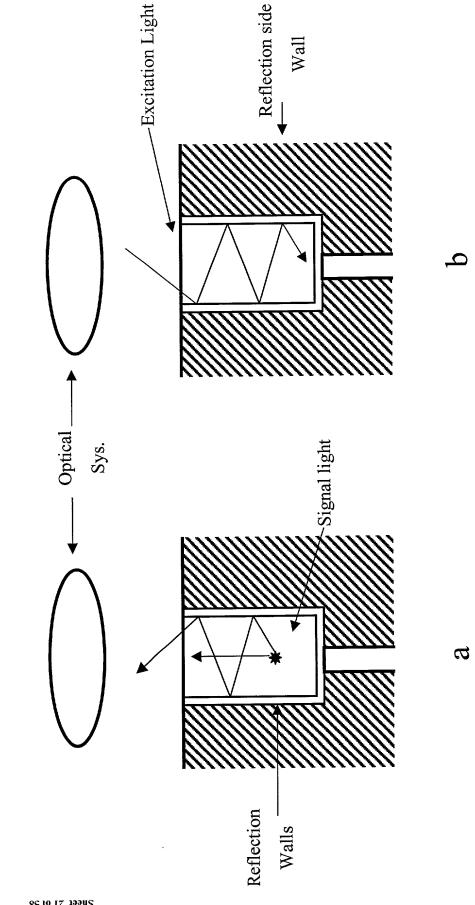


Fig.19. A method for reducing cross-contamination between adjacent holes during excess fluid removal

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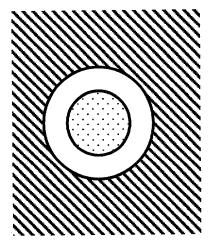
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Fig. 20 Use Reflection Wall of Reaction Chamber to Enhance Optical Signal of the Assay



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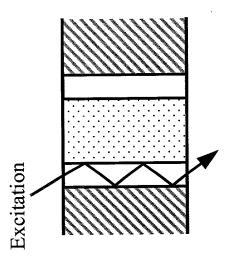


Fig21 Light guiding capillary

1. Immobilization on glass

n=0, 1, 8 R=-OH₃,-O₂H₃,-O₂H₄-

FIG. 22A

Blocking Step:

HS

other blocking options to be tested:

FIG 22B

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FIG. 22C

Process for tabrication using a negative mask Figure 23

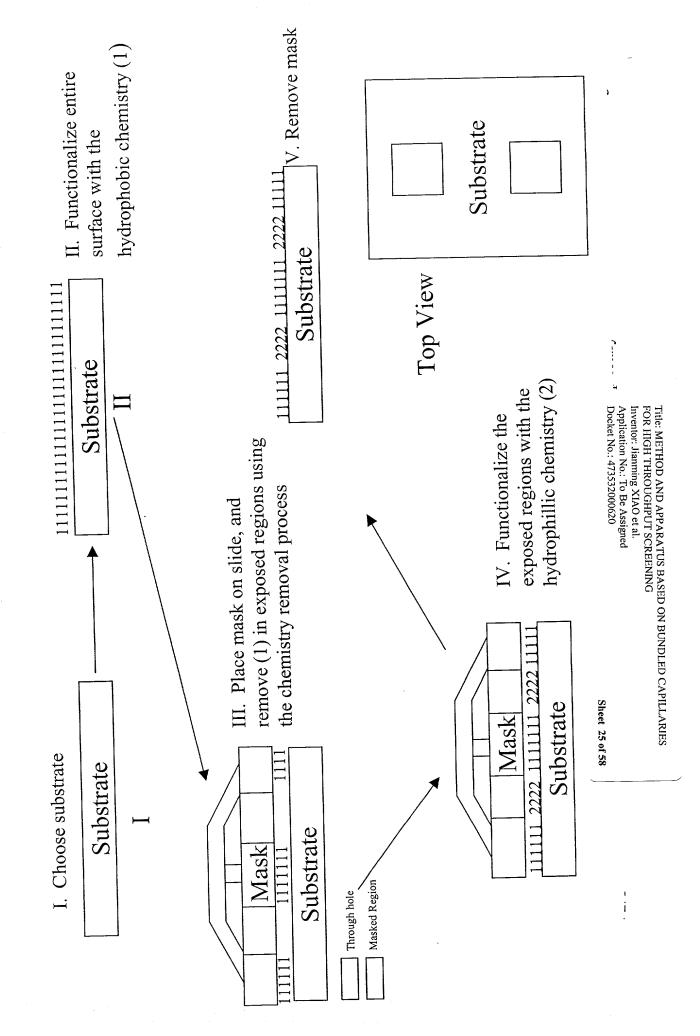


Figure 24 Process for the fabrication using positive mask

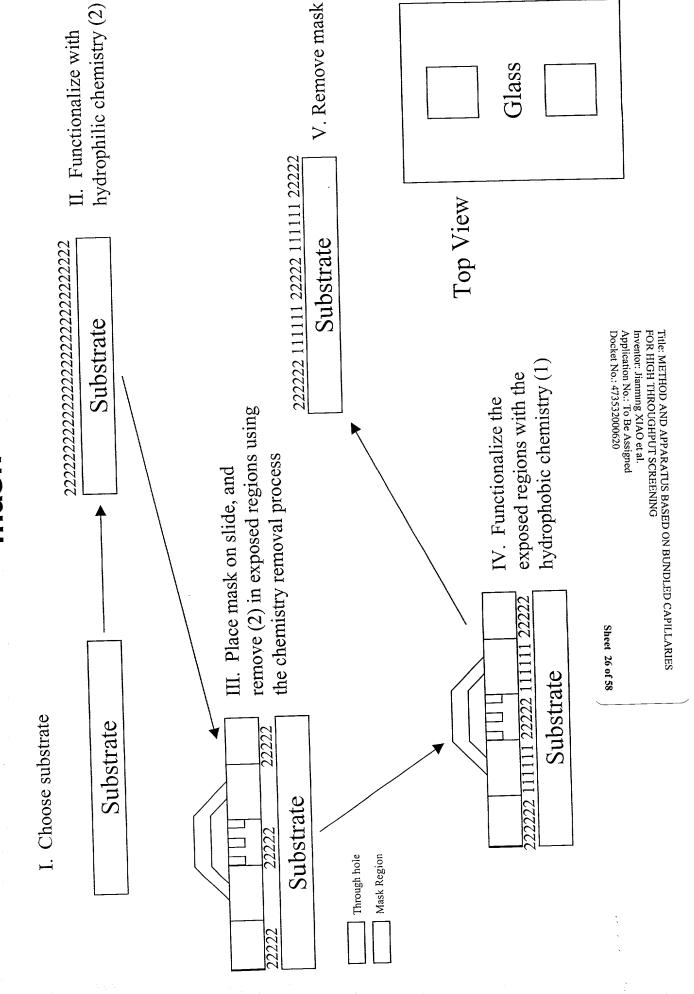


Figure 25 Chamber use

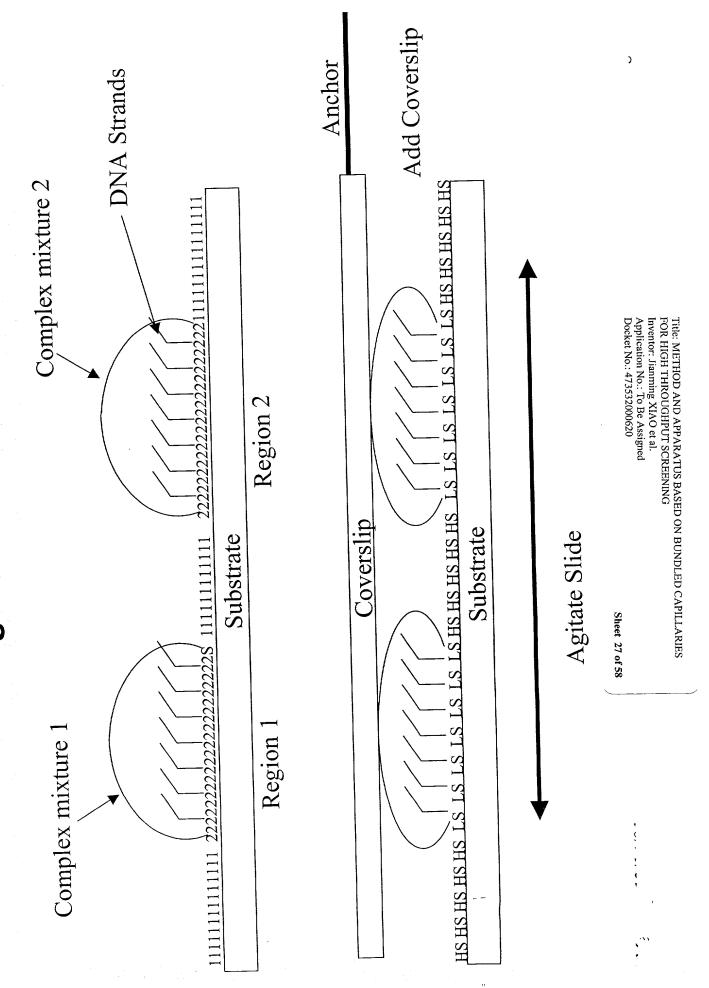
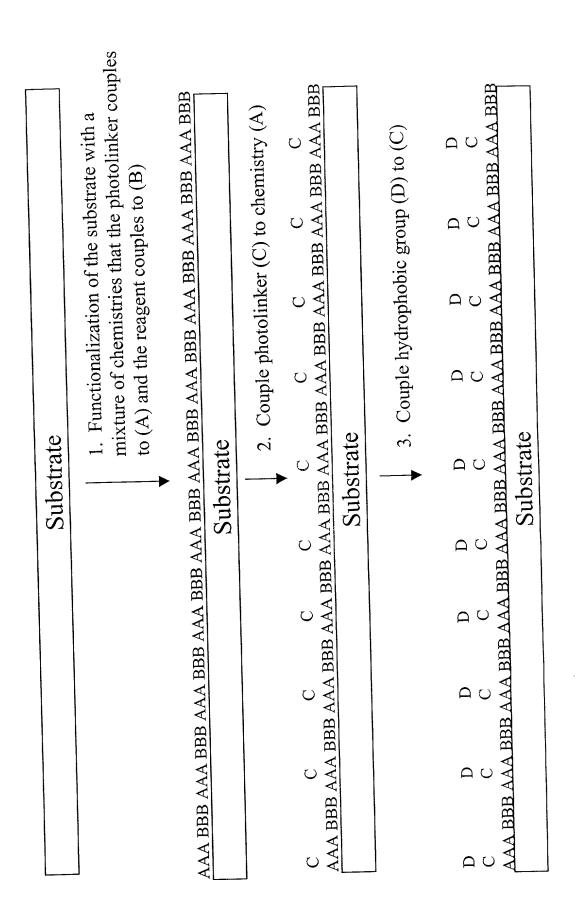


Figure 26A Surface Tension Patterning: On-capillary Fiber optic based patterning



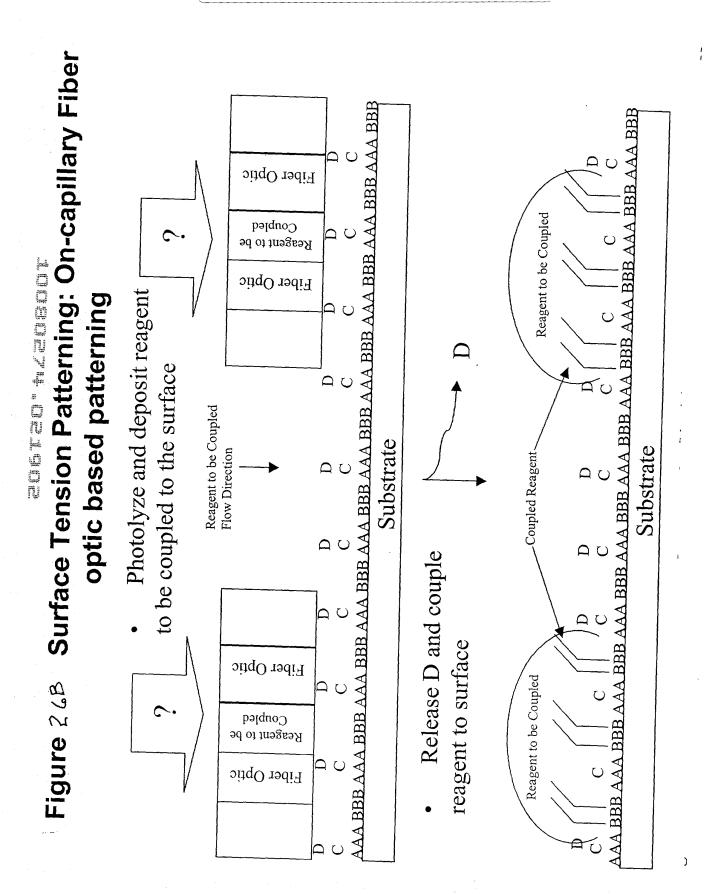
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Glass
Fiber Optic

Fiber Optic

Glass

Fiber Optic

Fiber Optic
Glass

Glass Fiber Optic

Fiber Optic

Glass

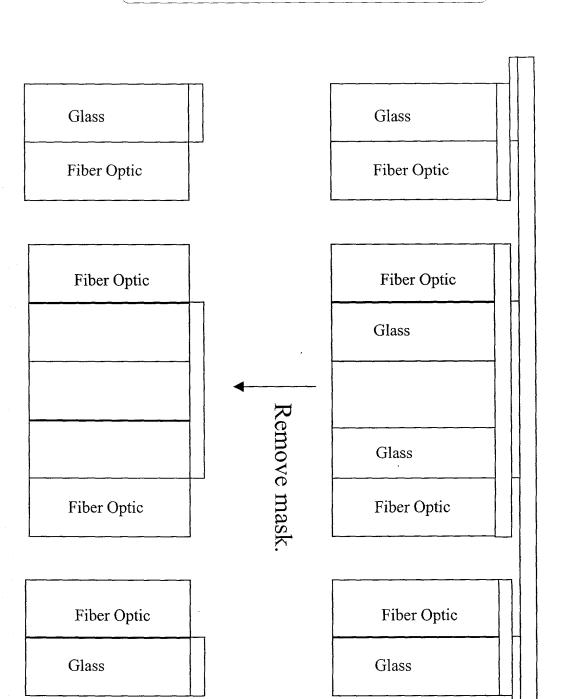
Glass

Fiber Optic

Fiber Optic Glass

Coat Surface with a Hydrophobic Reagent

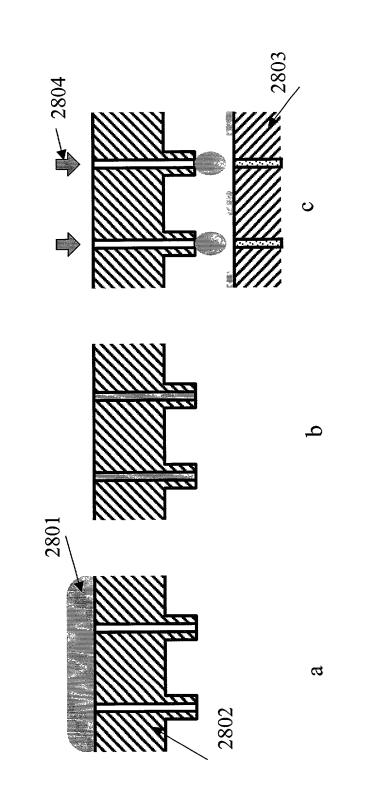
Volume Metering using Surface Tension Features



Place a Mask on to the Surface and Expose the Surface to the Chemistry Removal Process

Figure 278 Volume Metering using Surface Tension Features

Fig. 28 Reagent pre-metering using an intermediary through-hole array



2801 - reagent fluid applied in excessive; 2802 - intermediary through hole array;

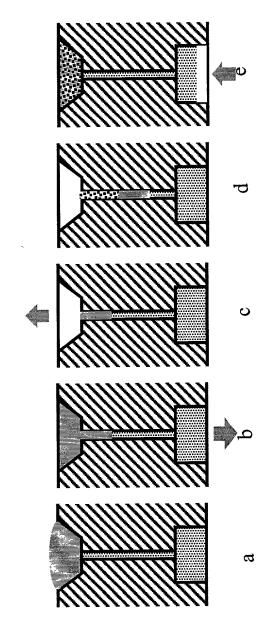
2803 - capillary array compound library;

2804 - pressure

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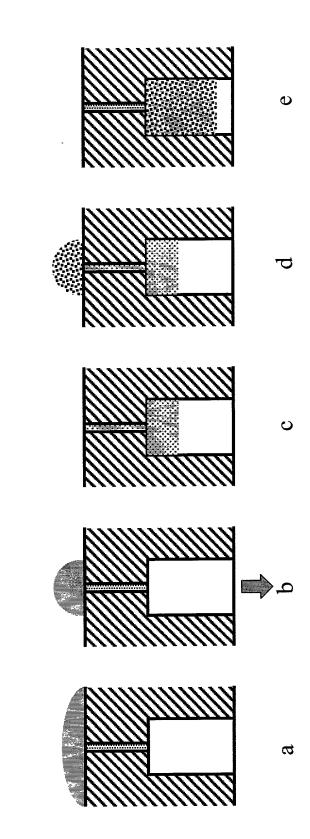
Fig. 29 Metering and mixing with a multi-use capillary array compound library



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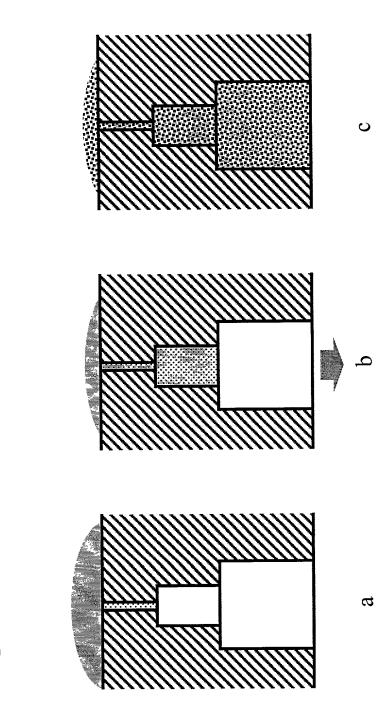
Fig. 30 Metering with hydrophilic patch and mixing



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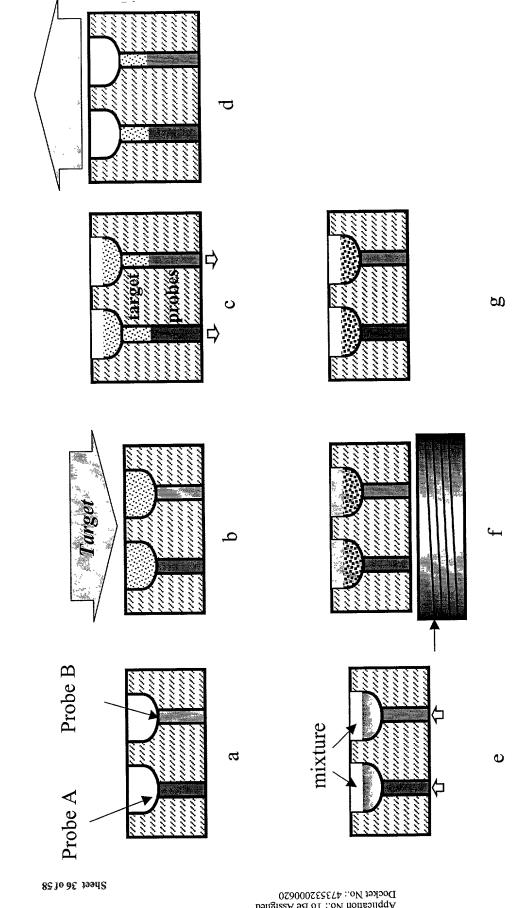
Fig. 31 Mixing and metering with interconnected chambers



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Fig. 32 Heterogeneous Assay



Antibody Immobilization via the Carbohydrate Moiety

. Oxidation of antibodies vicinal diol group to its aldehyde

2. Conjugation of maleimide moiety with antibody

3. Immobilization of the modified antibody to the surface.

FIG. 334

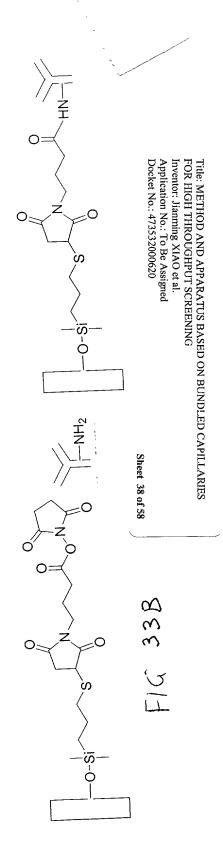
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Immobilization via Amine Goups

1. Hydrosilylation of (3-mercaptopropyl)triethoxysilane on the surface of fiber

2. Formation of a thioether bond

3. Attachment of fiber to antibody



Antibody Immobilization via Streptavidin

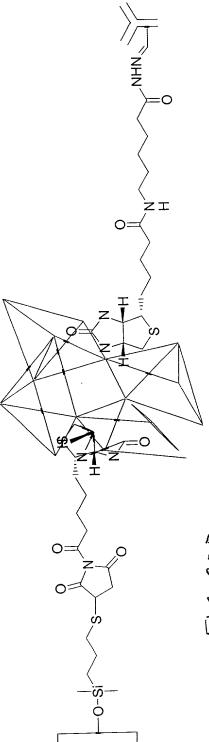
1. Label antibody with biotin

2. Modification of fiber surface with biotin maleimide

Antibody Immobilization via **Streptavidin**

3. Conjugate Streptavidin to the surface

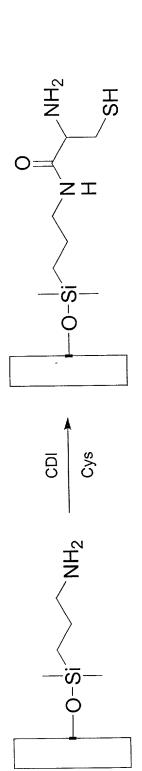
4. Conjugate Biotin Anitbody to the surface



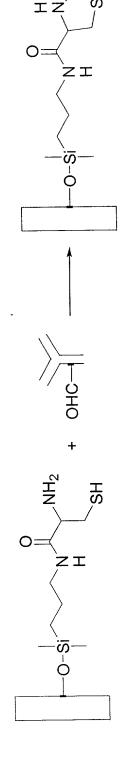
F16.33D

Formation of

. Surface attachment and formation of the linker



Thiazolidine formation رن آ



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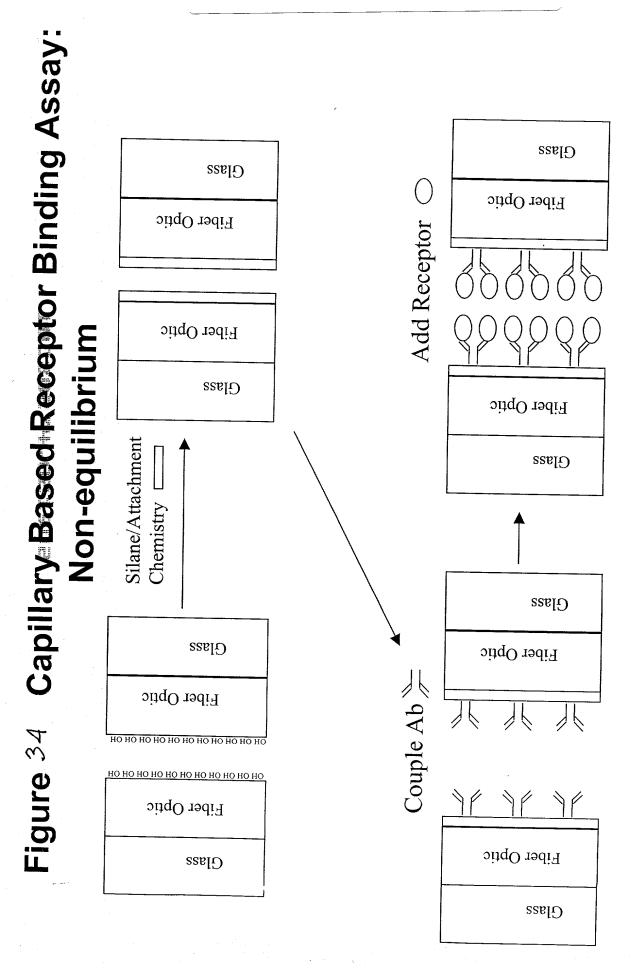
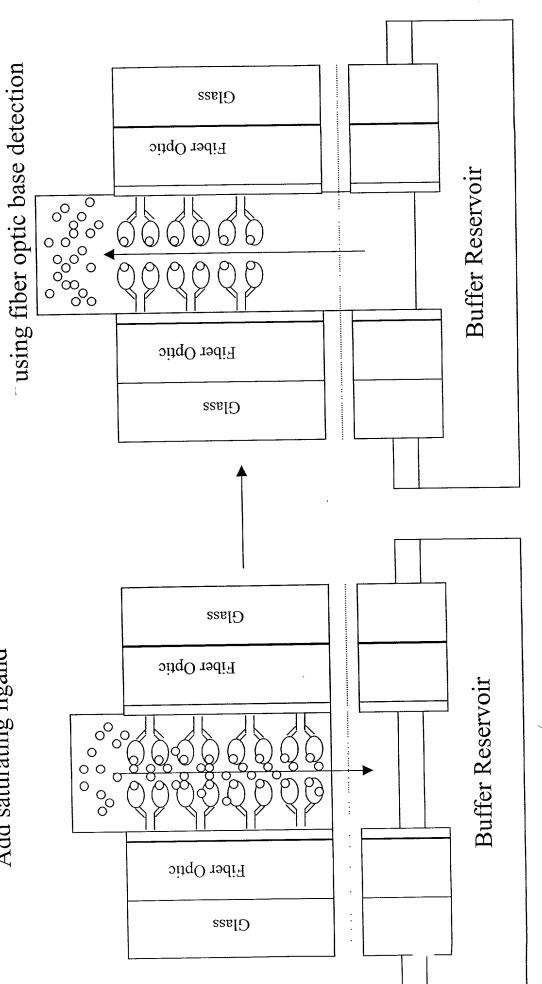


Figure 34 (cont. 1). Capillary Based Receptor Binding Wash unbound ligand Assay: Non-equilibrium

Add saturating ligand

and calculate total bound



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Figure 34 (cont. 2). Capillary Based Receptor Binding Assay: Non-equilibrium

optic based detection to observe Add compound and use fiber

. 0 8 0 0 0 0 0 Glass 0 0 O Reservoir Fiber Optic 0 000 00000 0 0 0 0 ~ Compound 800 0 0 صر رو 0 kinetics Fiber Optic 0 0 0 Inventor: Jranming XIAO et al.
Application No.: To Be Assigned
Docket No.: 473532000620 Tide: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES FOR HIGH THROUGHPUT SCREENING 0 Glass 0 00 0 Seompound Reservoir Glass Fiber Optic compound reservoir Sheet 44 of 58 Move capillary to Fiber Optic 0 ∞ Glass ∞ 8 O 0 0

igure 34 (cont. 3). Capillary Based Receptor Binding

Assay: Non-equilibrium

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Mover capillary to buffer reservoir and wash

Dry capillary

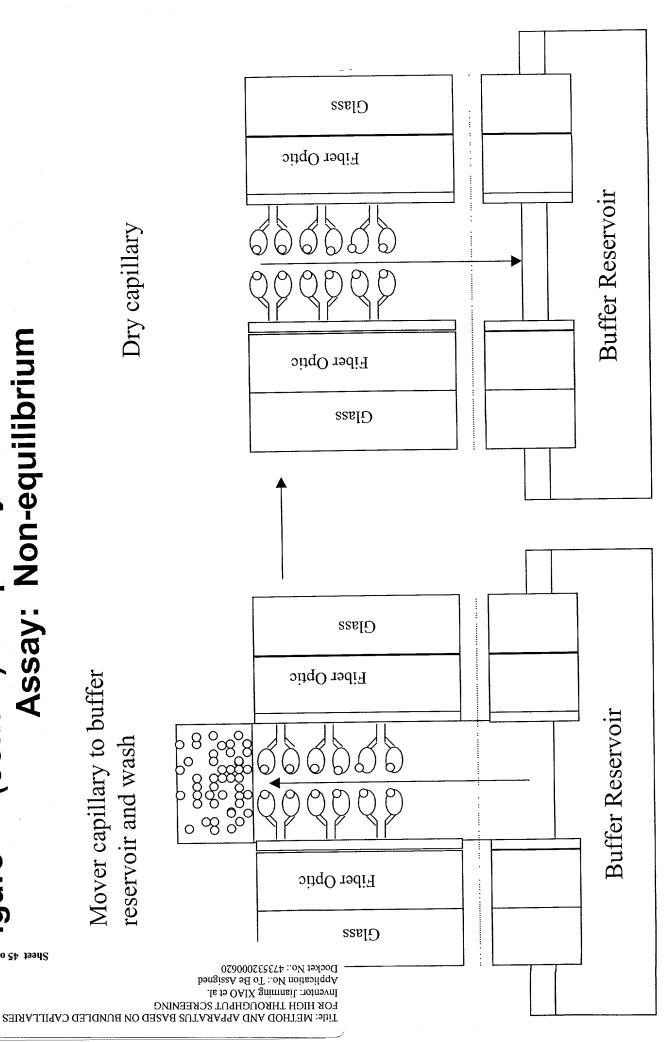
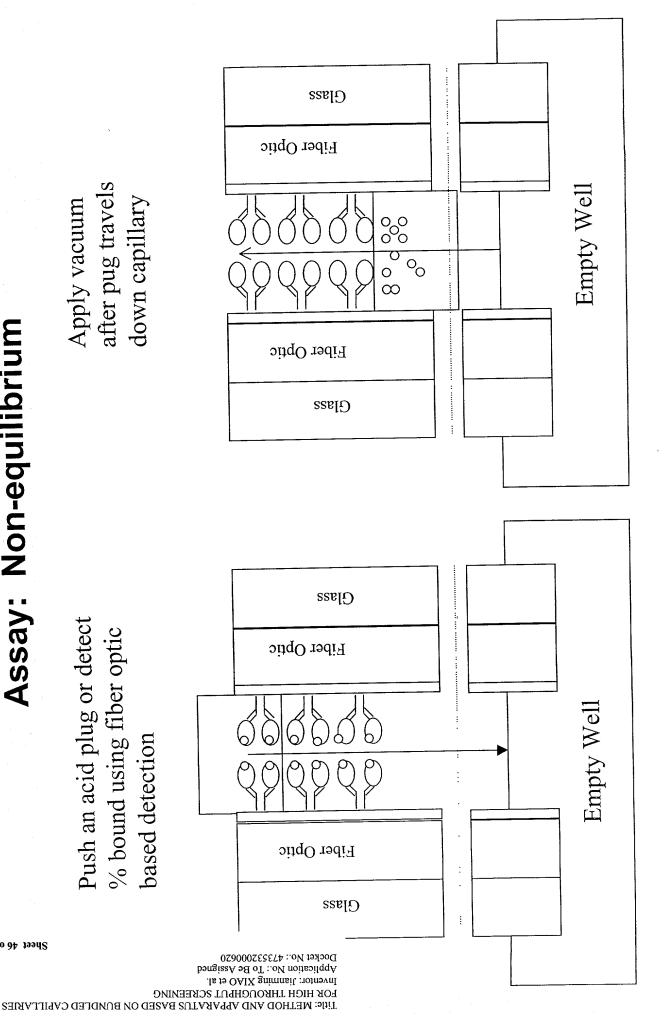


Figure 34 (cont. 4). Capillary Based Receptor Binding Assay: Non-equilibrium

Push an acid plug or detect % bound using fiber optic based detection

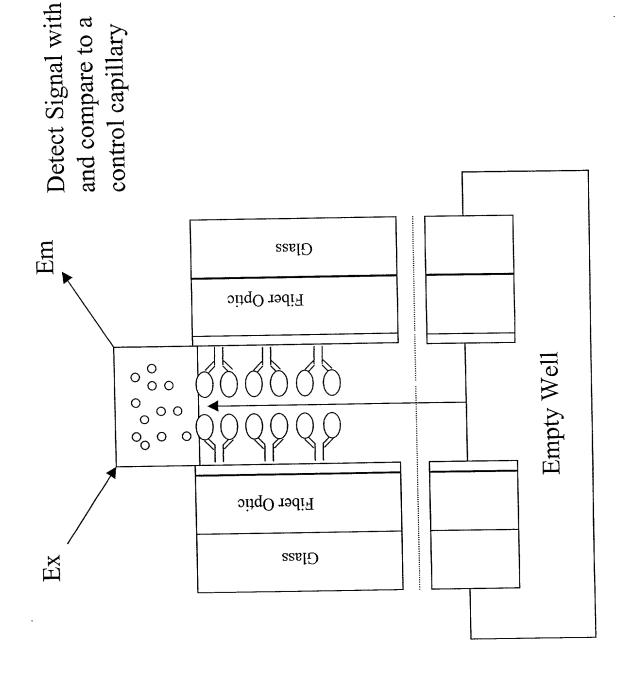
Apply vacuum after pug travels down capillary



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Figure 34 (cont. 5). Capillary Based Receptor Binding

Assay: non-equilibrium

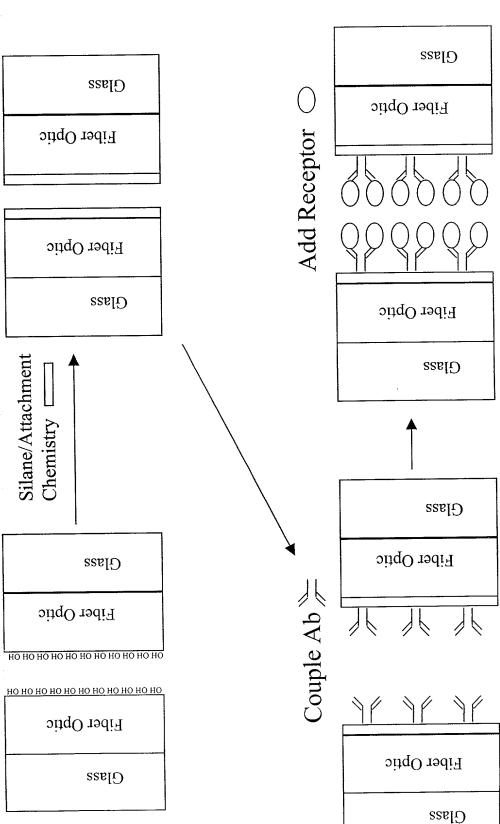


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Capillary Based Receptor Binding Assay: Figure 35

Equilibrium Silane/Attachment



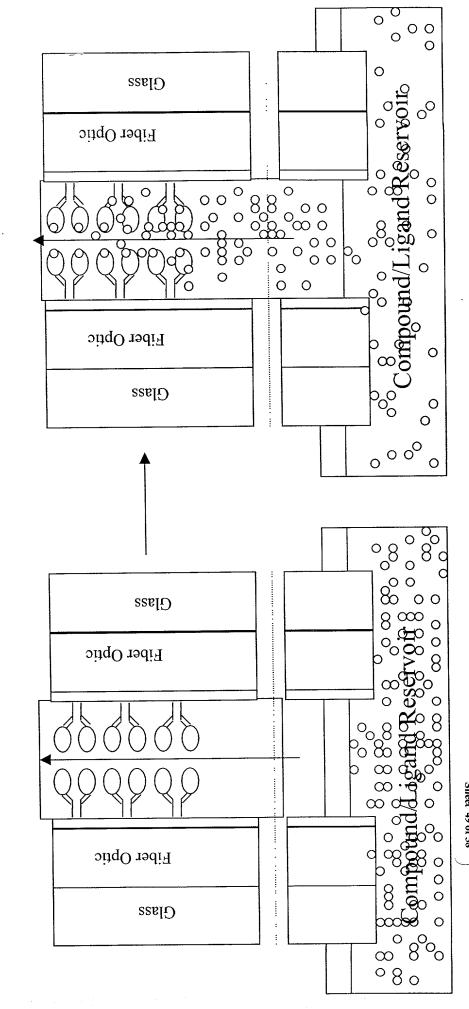
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Figure 35 (cont. 1). Capillary Based Receptor Binding Assay: Equilibrium

compound/ligand reservoir. Move Capillary to

Add solution and let system reach equilibrium. Detect equilibrium using fiber optic base detection.



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Figure 35 (cont. 2). Capillary Based Receptor Binding

Assay: Equilibrium

reservoir and wash capillary with buffer. Detect % bound using fiber optic based detection. Move capillary to a buffer Sheet 50 of 58

Dry Capillary

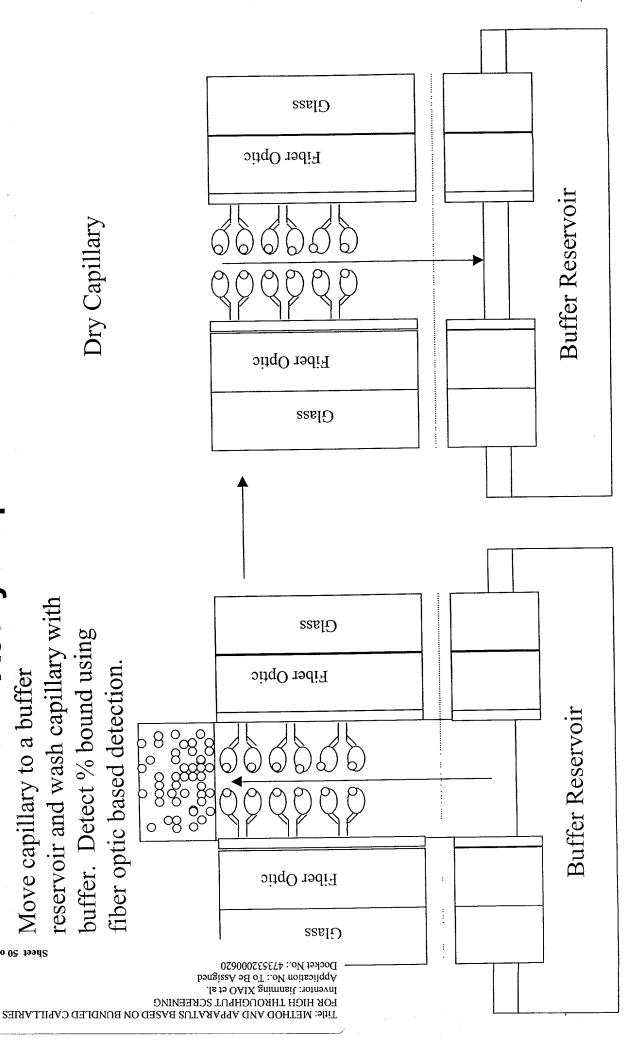


Figure 35 (cont. 3). Capillary Based Receptor Binding

Assay: Equilibrium

Detect signal using fiber optic base detection or elute bound ligand with acid.

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after pug travels down capillary Apply vacuum

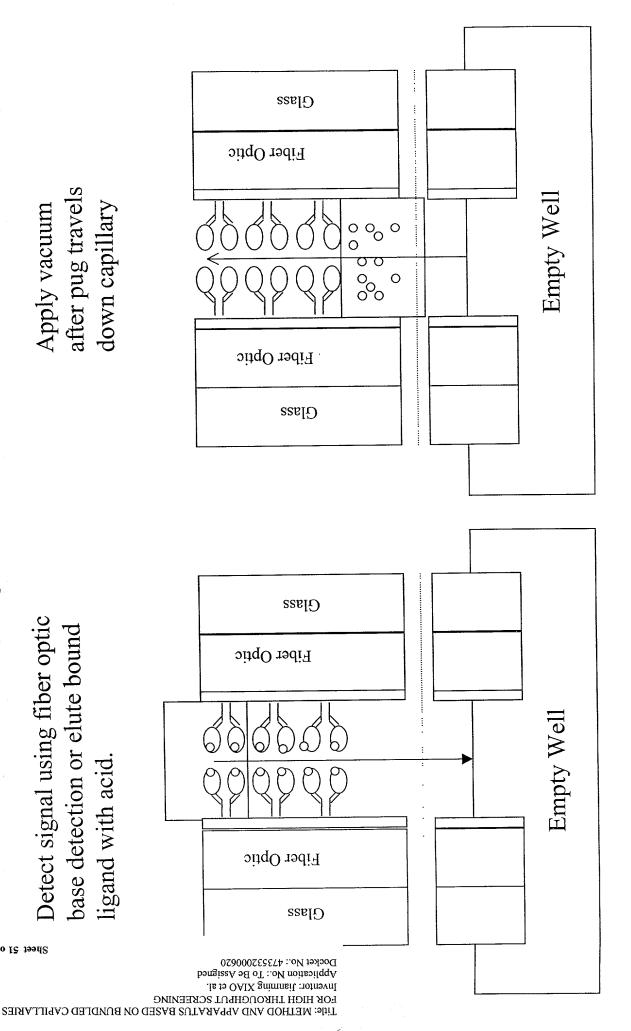
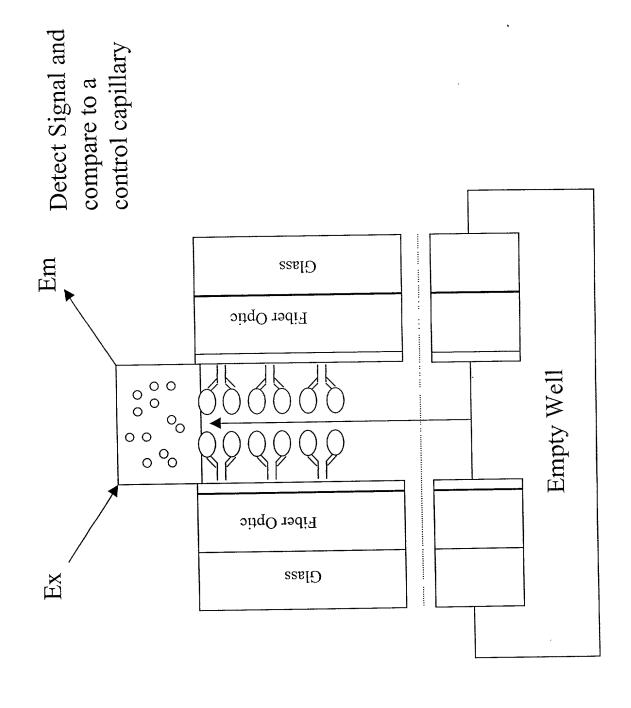


Figure 35 (cont. 4). Capillary Based Receptor Binding

Assay: Equilibrium

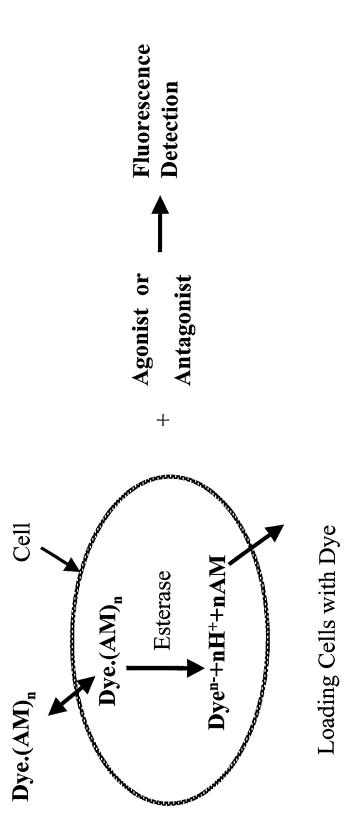


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Figure 36

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Assay Based on Tracking Cytosolic [Ca++]

Figure 37

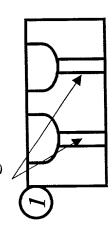
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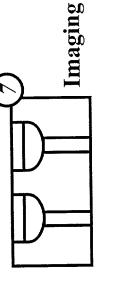
Protein Array & Cell Array

Example 1. Library of antigen or antibody

Attached to magnetic beads

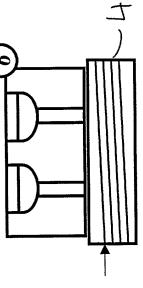


Aspiration from top



De-magnetize

Mixing circle



Seal Seal

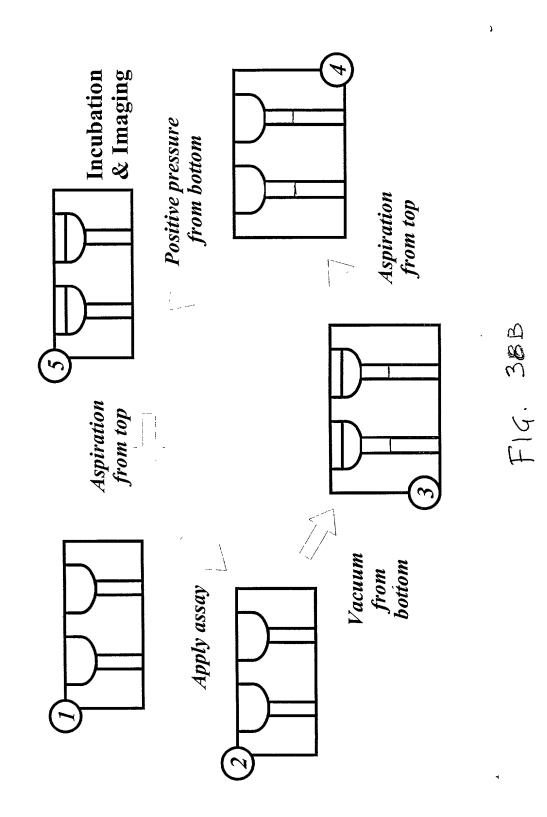
Magnetize & Washing circle

Binding interaction

3BA

F19.

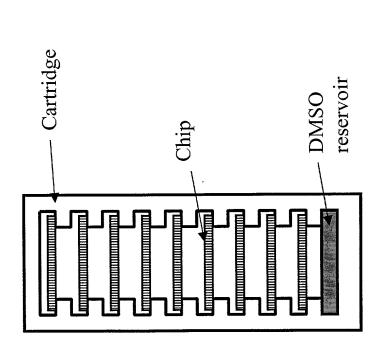
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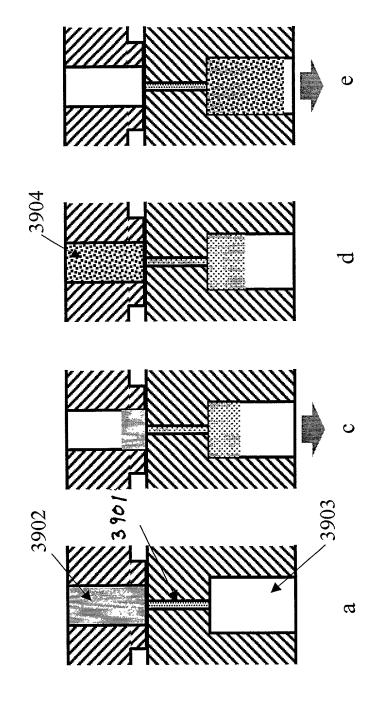
Fig. 39 One embodiment of the capillary array cartridge design



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Fig. ψ_0 Metering with through hole plates and mixing



3901 - compound and compound storage chamber

3902 - reagent A (i.e. enzyme) in through hole plate A

3903 – mixing/reaction chamber

3904 - reagent B (i.e. substrate) in through hole plate B

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